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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,152	02/01/2001	Chris C. Miller	RR-473PCT/US	1414

7590 02/23/2005

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EXAMINER

HAGHIGHATIAN, MINA

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,152

Applicant(s)

MILLER, CHRIS C.

Examiner

Mina Haghighatian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 70-99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 70-99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 February 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/04 has been entered.

Applicant's submission of amendments, remarks, Declaration of Dr. Neil Macintyre under 37 C.F.R. 1.132, and extension of time filed on 10/21/04 are also acknowledged.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

f) he did not himself invent the subject matter sought to be patented.

Claims 70-99 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

It appears that the instant invention was not invented by Mr. Chris Miller alone. In light of the letter of Mr. Miller addressed to Dr. Long, dated November 22, 1998, and submitted to the United State Patent and Trademark Office, it is concluded that Mr. Miller was not the sole inventor of the instant invention, as claimed.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 70 and 74-77 are rejected under 35 U.S.C. 102(b) as being anticipated by Green et al (WO 9509612).

Green teaches compositions capable of releasing nitric oxide and therapeutic methods of use thereof for the treatment of microorganism-related disease states. It is disclosed that **direct delivery** of nitric oxide **gas** kills intracellular pathogens such as *Mycobacterium tuberculosis*. An ability to specifically deliver compounds capable of releasing nitric oxide to the desired site of infection within the macrophage would greatly enhance killing of intracellular pathogens (page 5, lines 6-13).

Green discloses a method of inhibiting the proliferation of parasites, fungi, bacteria and other proliferating cells or organisms (page 7, lines 30-34). Also disclosed is that the nitric oxide releasing compounds, alone or in combination with other suitable components, can be made into aerosol formulations to be administered via inhalation (page 23, lines 7-10). *Administration through the aerosol route is highly beneficial* to humans or animals with pulmonary infections. Various bacterial, protozoan, fungal, viral and parasitic infections of the respiratory system that involve macrophages are attacked in this fashion (page 29, lines 15-25).

Green discloses that the dose administered to an animal, particularly a human, should be sufficient to effect a therapeutic response in the animal over reasonable time frame (page 24, line 30 to page 24, line 12).

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Claims 70-78 are rejected under 35 U.S.C. 102(b) as being anticipated by Bathe et al (5,558,083).

Bathe et al teaches a nitric oxide delivery system that is useable with any of a variety of gas delivery system that provides breathing gas to a patient. **Nitric oxide** in a diluent gas is delivered from a gas control valve (see abstract). Bathe discloses that the actual administration of NO is generally carried out by its introduction into the patient as a gas along with other normal inhalation gases given to the patient. Such commercially available supplies are provided in cylinders under pressure (col. 1, lines 20-34). The concentrations at or lower than 150 ppm are suggested (col. 1, lines 35-38).

Bathe discloses that nitric oxide is delivered using systems such as ventilation, where the NO is introduced by means of a gas proportioning device that provides a continuous flow to the patient. The invention includes a flow transducer that senses the flow of gas from the gas delivery system (col. 2, lines 13-30).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 70-94 and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bathe et al (5,558,083) in view of Green et al (WO 9509612).

Bathe et al and Green et al, were discussed above. Bathe et al teach a method of delivering nitric oxide gas to patients safely and effectively and Green et al teach the

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beneficial effects of killing the microorganisms of the respiratory system by exposing them directly to nitric oxide gas.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have combined the flow-controlled and diluted delivery of nitric oxide gas to patients for respiratory disorders with the teachings of Green et al on the effects of nitric oxide on killing and inhibiting the proliferation of extracellular microorganisms within the respiratory system of an animal because as disclosed nitric oxide can be very beneficial at therapeutic and safe concentration levels and where its delivery is monitored and controlled.

Claims 70-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zapol et al (5,873,359) in view of Green et al (WO 9509612).

Zapol et al teach a method of treating or preventing bronchoconstriction or reversible pulmonary vasoconstriction in a mammal, which method includes causing the mammal to inhale a therapeutically-effective concentration of gaseous nitric oxide or a therapeutically-effective amount of a nitric oxide releasing compound, and an inhaler device containing nitric oxide gas and/or nitric oxide-releasing compound (see abstract and summary of the invention).

Zapol discloses that the concentration of nitric oxide is at least 1 ppm, and more preferably at least 20 ppm and most preferably at least 80 ppm (see col. 4, lines 50-59). It is also disclosed that the Occupational Safety and Health Administration (OSHA) has

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set the time-weighted average inhalation limit for NO at 25 ppm for 10 hours (col. 3, lines 50-55), and that NO may be administered to mammals at a concentration of from 1 ppm to 40 ppm in air, pure oxygen or another suitable gas or gas mixture, for as long as needed (col. 11, lines 55-61). Zapol discloses that the nitric oxide is inhaled as a mixture including nitric oxide, oxygen and nitrogen gases (col. 4, lines 60-64). Zapol lacks disclosure on the effects of nitric oxide on microorganisms in the respiratory tract.

Green et al, discussed above, teach the beneficial effects of killing the microorganisms of the respiratory system by exposing them to nitric oxide gas.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have combined the method of safely and effectively delivering diluted nitric oxide gas to patients for respiratory disorders with the teachings of Green et al on the effects of nitric oxide on killing and inhibiting the proliferation of extracellular microorganisms within the respiratory system of an animal because as disclosed nitric oxide can be very beneficial at therapeutic and safe concentration levels and where its delivery is monitored and controlled.

Response to Arguments

Applicant's arguments with respect to claims 70-84 have been considered but are moot in view of the new ground(s) of rejection. However, since Green et al is still one of

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the references in the new rejection, arguments regarding the said reference will be addressed.

Applicant argues that Green does not disclose the inhalation of nitric oxide gas for killing, inhibiting or suppressing pathogenic microorganisms, but teaches use of generating compounds. Applicant also believes that Green is teaching against the use of nitric oxide gas. This is not commensurate with the scope of the claims. The instant claims do not require a delivery of nitric oxide gas directly to the respiratory system. In fact claims 70 and 79 recite "source of nitric oxide" and claim 76 recites "a nitric oxide substrate source containing a compound capable of producing nitric oxide". The specification also discloses that "nitric oxide source may be a compound, composition or substance producing nitric oxide" (see page 6, lines 7-8).

Applicant argues that Green does not teach the delivery of gaseous nitric oxide through inhalation. This is not commensurate with the scope of the claims. Instant claims require a source of nitric oxide and Green is disclosing a compound releasing nitric oxide gas directly onto the microorganism, which clearly meets the limitation of instant claims. Applicant insists that the instant claims are "limited to the inhalation of nitric oxide gas". This is not correct. Instant claims, especially claim 70 requires "Delivering the nitric oxide gas to the animal's respiratory tract THROUGH inhalation". In response it is disclosed that Green also has inhalation of compounds which Deliver nitric oxide gas to the animal's respiratory tract. Claim 70 also requires that "the inhalation of nitric oxide gas RESULTS in direct exposure of nitric oxide gas to the

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microorganism". Green also discloses that the generating compounds release nitric oxide gas directly onto the microorganisms.

Dr. MacIntyre's declaration has also been fully considered. It is considered persuasive with regard to claims 79-84, but not persuasive with regard to claims 70-78. Dr. MacIntyre describes Green et al's reference and compares green's disclosure with the instant invention. However Dr. MacIntyre is not considering the scope of the claims. The Office however, is examining the instant CLAIMS and Green is still considered a relevant art for claims 70 and 74-77 under anticipation and claims 70-94 and 97 under obviousness.

However, in response to the Applicant's remarks and the Declaration, it appeared that the rejection should be altered to constitute Bathe et al as the primary reference and Green et al as the supporting prior art.

Bathe et al is clearly teaching a method of safely and effectively administering diluted nitric oxide gas directly and via inhalation to a patient's respiratory system. Green is relied upon its teaching on the beneficial effects of nitric oxide for killing and inhibiting proliferation of microorganisms within the respiratory system.

It is considered that a combination of Bathe et al and Green et al provides sufficient disclosure to one of ordinary skill in the art to make and use the invention as claimed.

For further clarity it is also disclosed that although Bathe et al does not specifically disclose a method of killing or inhibiting the proliferation of extracellular microorganisms within the respiratory tract of an animal, it is considered that the

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disclosure of Bathe et al on administration of nitric oxide gas to a patient's respiratory system meets such limitations of the claims. This is so because all patients are considered to have a number of microorganisms in their respiratory system, and while the scope of the claims 70-78 does not specifically limit the method to patients with infections, it is considered that Bathe et al is inherently meeting the limitations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

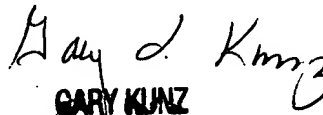
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L. Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mina Haghighatian
February 09, 2005


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